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09/848,841	05/04/2001	Karlene H. Butler	BB1252 USNA1	8694

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EXAMINER	
KUBELIK, ANNE R	

ART UNIT	PAPER NUMBER
1638	

DATE MAILED: 02/26/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Application No.	Applicant(s)
09/848,841	BUTLER ET AL.
Examiner	**Art Unit**
Anne R. Kubelik	1638

Office Action Summary

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED. (35 U.S.C. § 133)
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *26 November 2002*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-6 and 24-32* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-6 and 24-32* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *with the application* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a)☐ The translation of the foreign language provisional application has been received.

15)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1)☒ Notice of References Cited (PTO-892)
2)☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3)☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *4,5*.
4)☐ Interview Summary (PTO-413) Paper No(s). _____.
5)☐ Notice of Informal Patent Application (PTO-152)
6)☐ Other:

DETAILED ACTION

1. Applicant's election with traverse of Group I and SEQ ID NOs:3, 11 and 15 in Paper No. 8 is acknowledged. The traversal is on the ground(s) that SEQ ID NOs:3 and 11 are portions of SEQ ID NO:15. These arguments are accepted as far as SEQ ID NOs:3, 11 and 15 are concerned. Claims 1-6 and 24-32 are pending.

The restriction requirement with respect to the other sequences is still deemed proper and is therefore made FINAL.

2. The application data sheet/declaration is defective. A new oath or declaration or Application Data Sheet in compliance with 37 CFR 1.67(a) identifying this application by application number and filing date is required. See MPEP §§ 602.01 and 602.02.

The Application Data Sheet/Declaration is defective because:

a. The name of the 7th inventor differs between the Application Data Sheet and the Declaration. On the Declaration, the name is Zhan-Bin Liu, while on the Application Data Sheet that inventor's name is Zhan-Bin Li.

b. The instant application is claimed as a continuation of PCT application PCT/US99/25953 in the Application Data Sheet and as a continuation-in-part of the PCT application in the first paragraph of the application.

c. The filing date of PCT application PCT/US99/25953 is incorrectly listed in the Application Data Sheet.

3. Applicant has not complied with one or more conditions for receiving the benefit of an earlier filing date under 35 U.S.C. 120 as follows: the instant application is claimed as a continuation of PCT application PCT/US99/25953 in the Application Data Sheet and as a

continuation-in-part of the PCT application in the first paragraph of the application, as discussed above. Correction is required.

4. The title of the invention is not descriptive of the instant invention, which is a nucleic acid encoding an NPR1 from rice, a method of using it to alter pathogen resistance in a plant, and plants, cells and viruses comprising recombinant DNA constructs comprising the nucleic acid. A new title is required that is clearly indicative of the invention to which the claims are directed. Note that titles can be up to 500 characters long.

5. The abstract is not descriptive of the instant invention, which is a nucleic acid encoding an NPR1 from rice, a method of using it to alter pathogen resistance in a plant, and plants, cells and viruses comprising recombinant DNA constructs comprising the nucleic acid. A new abstract is required that is clearly indicative of the invention to which the claims are directed. The abstract of the disclosure should describe the disclosure sufficiently to assist readers in deciding whether there is a need for consulting the full patent text for details.

6. The disclosure is objected to because of the following informalities: pg 15, lines 20-21, of the specification reads "at least XXX amino acids that has at least XX% identity".

Appropriate correction, without introduction of new matter, is required.

Claim Objections

7. Claims 31-32 are objected to because of the following informalities:

The claims are missing an article before "recombinant" in line 2.

Claim Rejections - 35 USC § 112

8. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

9. Claims 1-6 and 24-32 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for nucleic acids encoding SEQ ID NO:16, vectors, cells and plants comprising the nucleic acid and methods of using it to alter the level of pathogen resistance in a plant, does not reasonably provide enablement for nucleic acids of SEQ ID NOs:4 or 12 or encoding proteins with 80% identity to SEQ ID NO:4, 12 or 16, vectors, cells and plants comprising those nucleic acids, and methods of using them to alter the level of pathogen resistance in a plant. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention commensurate in scope with these claims.

The claims are broadly drawn to nucleic acids encoding NPR1 proteins with 80% identity to SEQ ID NO:4, 12 or 16, vectors, cells and plants comprising the nucleic acids, and methods of using them to alter the level of pathogen resistance in a plant.

The instant specification, however, only provides guidance for sequencing cDNA libraries from corn, rice and wheat (example 1); BLAST analysis of the sequences (example 2) to identify those with homology to Arabidopsis NPR1 (example 3). The rice sequences are SEQ ID NOs:3, 11 and 15, which encode SEQ ID NOs:4, 12 and 16, respectively; SEQ ID NOs:3 and 11 are partial sequences of SEQ ID NO:15 (example 3). The specification also provides general

guidance for expression of genes in monocots (example 4), dicots (example 5), and bacteria (example 6).

The instant specification fails to provide guidance for nucleic acids encoding NPR1 proteins with 80% identity to SEQ ID NO:4, 12 or 16, vectors, cells and plants comprising the nucleic acids, and methods of using them to alter the level of pathogen resistance in a plant.

The instant specification fails to provide guidance for construction or isolation of NPR1-encoding nucleic acids other than SEQ ID NOs:4, 12 and 16. No guidance is provided, for example, for the exact hybridization or amplification conditions and probes/primers to use in isolation of nucleic acids other than SEQ ID NOs:4, 12 and 16.

The specification, on pg 6, lines 4-16 suggests making variants in which codons for "chemically equivalent amino acids" are substituted for codons for existing amino acids in the encoded proteins. Making such "conservative" substitutions (*e.g.*, substituting one polar amino acid for another, or one acidic one for another) does not produce predictable results. Lazar et al (1988, Mol. Cell. Biol. 8:1247-1252) showed that the "conservative" substitution of glutamic acid for aspartic acid at position 47 reduced biological function of transforming growth factor alpha while "nonconservative" substitutions with alanine or asparagine had no effect (abstract). Similarly, Hill et al (1998, Biochem. Biophys. Res. Comm. 244:573-577) teach that when three histidines that are maintained in ADP-glucose pyrophosphorylase across several species are substituted with the "nonconservative" amino acid glutamine, there is little effect on enzyme activity, while the substitution of one of those histidines with the "conservative" amino acid arginine drastically reduced enzyme activity (see Table 1). All these mutated proteins would have at least a high percent identity to the original protein.

Given the claim breath, unpredictability, and lack of guidance as discussed above, undue experimentation would have been required by one skilled in the art to develop and evaluate nucleic acids encoding NPR1 proteins with 80% identity to SEQ ID NO:16. Making all possible single amino acid substitutions in an X593 amino acid long protein like that encoded by SEQ ID NO:16 would require making and analyzing 19^{593} nucleic acids; these proteins would have 99.8% identity to SEQ ID NO:16. Because nucleic acids encoding proteins with 80% identity to SEQ ID NO:16 would encode proteins with 118 amino acid substitutions, many more than 19^{593} nucleic acids would need to be made and analyzed.

As the specification does not describe the transformation of any plant with a nucleic acid encoding an NPR1 protein with 80% identity to SEQ ID NO:4, 12 or 16, undue trial and error experimentation would be required to screen through the myriad of nucleic acids encompassed by the claims and plants transformed therewith, to identify those with altered pathogen resistance, if such plants are even obtainable.

SEQ ID NOs:3 and 11 encode fragments of the protein encoded by SEQ ID NO:15. Neither SEQ ID NO:3 nor 11 encode the first 172 amino acids of the rice NPR1 protein, including the starting methionine, and SEQ ID NO:3 does not encode the nuclear localization signal required for activation of pathogenesis-related genes (see Kinkema et al. 2000, Plant Cell 12:2339-2350, paragraph spanning pg 2342-2343 and pg 2344, right column, paragraph 2, to pg 2345, right column, paragraph 1). The specification does not teach how to use nucleic acids encoding only portions of the rice NPR1 protein.

Given the claim breath, unpredictability in the art, undue experimentation, and lack of guidance in the specification as discussed above, the instant invention is not enabled throughout the full scope of the claims.

10. Claims 1-6 and 24-32 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter that was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The claims are broadly drawn to a multitude of DNA molecules that have encode proteins with 80% identity to SEQ ID NOs:4, 12 or 16 and that have NPR1 activity. In contrast, the specification only describes nucleic acids from rice that comprise SEQ ID NO: 4, 12 and 16. Applicant does not describe other DNA molecules encompassed by the claims, and the structural features that distinguish all such nucleic acids from other nucleic acids are not provided.

Hence, Applicant has not, in fact, described DNA molecules that encode proteins with 80% identity to SEQ ID NOs:4, 12 or 16 and that have NPR1 activity within the full scope of the claims, and the specification fails to provide an adequate written description of the claimed invention.

Therefore, given the lack of written description in the specification with regard to the structural and physical characteristics of the claimed compositions, it is not clear that Applicant was in possession of the genus claimed at the time this application was filed.

See *Univ. of California v. Eli Lilly*, 119 F.3d 1559, 43 USPQ 2d 1398 (Fed. Cir. 1997):

> The name cDNA is not in itself a written description of that DNA; it conveys no distinguishing information concerning its identity. While the example provides a process for obtaining human insulin-encoding cDNA, there is no further information in the patent pertaining to that cDNA's relevant structural or physical characteristics; in other words, it thus does not describe human insulin cDNA .... Accordingly, the specification does not provide a written description of the invention ....

and at pg 1406:

> a generic statement such as "vertebrate insulin cDNA" or "mammalian insulin cDNA," without more, is not an adequate written description of the genus because it does not distinguish the genus from others, except by function. It does not specifically define any of the genes that fall within its definition. It does not define any structural features commonly possessed by members of the genus that distinguish them from others. One skilled in the art therefore cannot, as one can do with a fully described genus, visualize or recognize the identity of the members of the genus. A definition by function, as we have previously indicted, does not suffice to define the genus because it is only an indication of what the genes does, not what it is

See *Amgen Inc. v. Chugai Pharmaceutical Co. Ltd.*, 18 USPQ 2d 1016 at page 1021:

> A gene is a chemical compound, albeit a complex one, and ... conception of a chemical compound requires that the inventor be able to define it so as to distinguish it from other materials .... Conception does not occur unless one has a mental picture of the structure of the chemical or is able to define it by its method of preparation, its physical or chemical properties, or whatever characteristics sufficiently distinguish it. It is not sufficient to define it solely by it principal biological property, *e.g.*, encoding human erythropoietin, because an alleged conception having no more specificity than that is simply a wish to know the identity of any material with that biological property.

11. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

12. Claim 25 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter that Applicant regards as the invention. Dependent claims are included in all rejections.

Claim 25 is rejected under 35 U.S.C. 112, second paragraph, as being incomplete for omitting essential steps, such omission amounting to a gap between the steps. See MPEP § 2172.01. The method is one of altering the level of pathogen resistance in a plant. The omitted steps are those involved in the regeneration of a plant from the plant cell. Step (c) maintains the plant cell in conditions suitable for development into a plant, but such development does not seem to occur in that step or any others. Additionally, it is not clear what one does with the

comparison of resistance in the plant cell in part (d) and how that alters the level of pathogen resistance in a plant.

Claim Rejections - 35 USC § 102

13. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.

14. The provisional application from which the instant application claims priority, 60/107,242, filed 5 November 1998, only provides support for SEQ ID NOs:3/4. The PCT application of which the instant application is a continuation-in-part, PCT/US99/25953, filed 4 November 1999, only provides support for SEQ ID NOs:11/12; in the PCT application these sequences are SEQ ID NOs:5/6. Thus, the priority date for SEQ ID NOs:3/4 is 5 November 1998; for SEQ ID NOs:11/12 it is 4 November 1999; and for SEQ ID NOs:15/16 it is 4 May 2001, the filing date of the instant application.

15. Claims 1-6 and 24-32 are rejected under 35 U.S.C. 102(a) as being anticipated by Bourgri et al (WO00/70069).

Bourgri et al teach a rice nucleic acid that encodes a protein with 99.6% identity to SEQ ID NO:16; the nucleic acid that encodes this protein has 99.4% identity to SEQ ID NO:15 (see sequence search results). This nucleic acid encodes an NPR1 homolog (pg 27-31). Bourgri et al also teach *Agrobacterium*-mediated and particle gun-mediated transformation of wheat and rice cells and plants with vectors, including viruses, comprising this nucleic acid including vectors in

which the nucleic acid is operably linked to the 35S promoter and the nos terminator (pg 10, lines 21-25, pg 43-50, and claims 1-17); the resulting plants are more resistant to disease than are untransformed plants (pg 50-53 and claims 33-34).

Conclusion

16. No claim is allowed.

17. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Anne R. Kubelik, whose telephone number is (703) 308-5059. The examiner can normally be reached Monday through Friday, 8:30 am - 5:00 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Amy Nelson, can be reached at (703) 306-3218. The fax phone numbers for the organization where this application or proceeding is assigned are (703) 872-9306 for regular communications and (703) 872-9307 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to Customer Service at (703) 308-0198.

Anne R. Kubelik, Ph.D.
January 29, 2003